

human origin.

- 5
9. The chimeric protein of claim 8, wherein the human insulin precursor is capable of being bound by an anti-human-insulin antibody.
10. The chimeric protein of claim 8, wherein the human insulin precursor consists of the amino acid sequence of SEQ ID NO:4.
- 10 11. The chimeric protein of claim 8, wherein in the human insulin precursor, B chain and A chain of the human insulin precursor are separated by an amino acid residue or a peptidyl fragment consisting of 2 to 34 amino acid residues.
- 15 12. The chimeric protein of claim 8, wherein the human insulin precursor consists of the amino acid sequence of SEQ ID NO:5.
13. A chimeric protein consisting of the amino acid sequence of SEQ ID NO:6.
- 20 14. A chimeric protein consisting of the amino acid sequence of SEQ ID NO:7.
15. An isolated nucleic acid comprising a nucleotide sequence encoding the chimeric protein of claim 1.
- 25 16. An isolated nucleic acid comprising a nucleotide sequence encoding the chimeric protein of claim 13.
17. An isolated nucleic acid comprising a nucleotide sequence encoding the chimeric protein of claim 14.
- 30 18. The nucleic acid of claim 15, wherein said nucleic acid is a DNA.
19. An isolated nucleic acid comprising a nucleotide sequence complementary to the nucleotide sequence of claim 15.
- 35 20. An isolated nucleic acid hybridizable to the nucleotide sequence

encoding the first, second and third peptidyl fragments of the DNA of claim 18.

21. A recombinant cell containing the nucleic acid of claim 15.
- 5 22. A recombinant cell containing the nucleic acid of claim 16.
23. A recombinant cell containing the nucleic acid of claim 17.
24. A method of producing a chimeric protein comprising growing a  
10 recombinant cell containing the nucleic acid of claim 15 such that the encoded chimeric protein is expressed by the cell, and recovering the expressed chimeric protein.
25. A method of producing a chimeric protein comprising growing a  
15 recombinant cell containing the nucleic acid of claim 16 such that the encoded chimeric protein is expressed by the cell, and recovering the expressed chimeric protein.
26. A method of producing a chimeric protein comprising growing a  
20 recombinant cell containing the nucleic acid of claim 17 such that the encoded chimeric protein is expressed by the cell, and recovering the expressed chimeric protein.
27. The product of the process of claim 24.
28. The product of the process of claim 25.
- 25 29. The product of the process of claim 26.
30. A process for obtaining a correctly folded first insulin-precursor-containing chimeric protein, comprising contacting an incorrectly folded second insulin-precursor-containing chimeric protein, which said second insulin-precursor-containing  
30 chimeric protein consists of an intramolecular chaperone (IMC) like peptidyl fragment separated from the insulin precursor by one or more cleavable amino acid residues, with at least one chaotropic auxiliary agent in an aqueous medium; wherein said IMC like peptidyl fragment:
- 35 a) contains from about 20 to about 200 amino acid residues;  
b) is not the insulin precursor or a portion thereof; and  
c) improves the insulin precursor folding such that the yield of the correctly

folded first insulin-precursor-containing chimeric protein when the incorrectly folded second insulin-precursor-containing chimeric protein is contacted with the chaotropic auxiliary agent is higher than the yield of the correctly folded insulin precursor when the incorrectly folded insulin precursor, which does not contain said IMC like peptidyl fragment, is contacted with the same chaotropic auxiliary agent.

5

31. The process of claim 30, wherein the insulin precursor is of human origin.

10

32. The process of claim 31, wherein the human insulin precursor is capable of being bound by an anti-human-insulin antibody.

33. The process of claim 31, wherein the human insulin precursor consists of the amino acid sequence of SEQ ID NO:4.

15

34. The process of claim 31, wherein in the human insulin precursor, B chain and A chain of the human insulin precursor are separated by an amino acid residue or a peptidyl fragment consisting of 2 to 34 amino acid residues.

20

35. The process of claim 31, wherein the human insulin precursor consists of the amino acid sequence of SEQ ID NO:5.

36. The process of claim 30, wherein the IMC like peptidyl fragment contains higher percentage of charged amino acid residue than the insulin precursor.

25

37. The process of claim 30, wherein in the IMC like peptidyl fragment, the N-terminal half contains more positively charged amino acid residues than negatively charged amino acid residues and the C-terminal half contains more negatively charged amino acid residues than positively charged amino acid residues.

30

38. The process of claim 30, wherein the IMC like peptidyl fragment consists of an amino acid sequence that has at least 40% identity to a domain containing at least first 20 N-terminal amino acids of human growth hormone (hGH) protein, in which the percentage identity is determined over an amino acid sequence of identical size to the domain of hGH.

35